M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: October 5, 1999

To: Dockets Management Branch (HFA-305)

From: Melissa Lamb
Office of Generic Drugs

Subject: OGD Update on the Review Process and New FDA Initiatives

This memorandum forwards overheads of a presentation to the Dockets Management Branch for inclusion in Docket 90S-0308. The following is information on the presentation for the Docket records:

Title of Presentation: OGD Update on the Review Process and New FDA Initiatives

Presented for: Regulatory Affairs Professionals Society Annual Conference

Date Presented: 10/5/1999

Presented by: Gary J. Buehler

Number of Pages: 22

Melissa Lamb

Attachment

90S-0308

M612

Regulatory Affairs Professionals Society Annual Conference

OGD Update on the Review Process and New FDA Initiatives

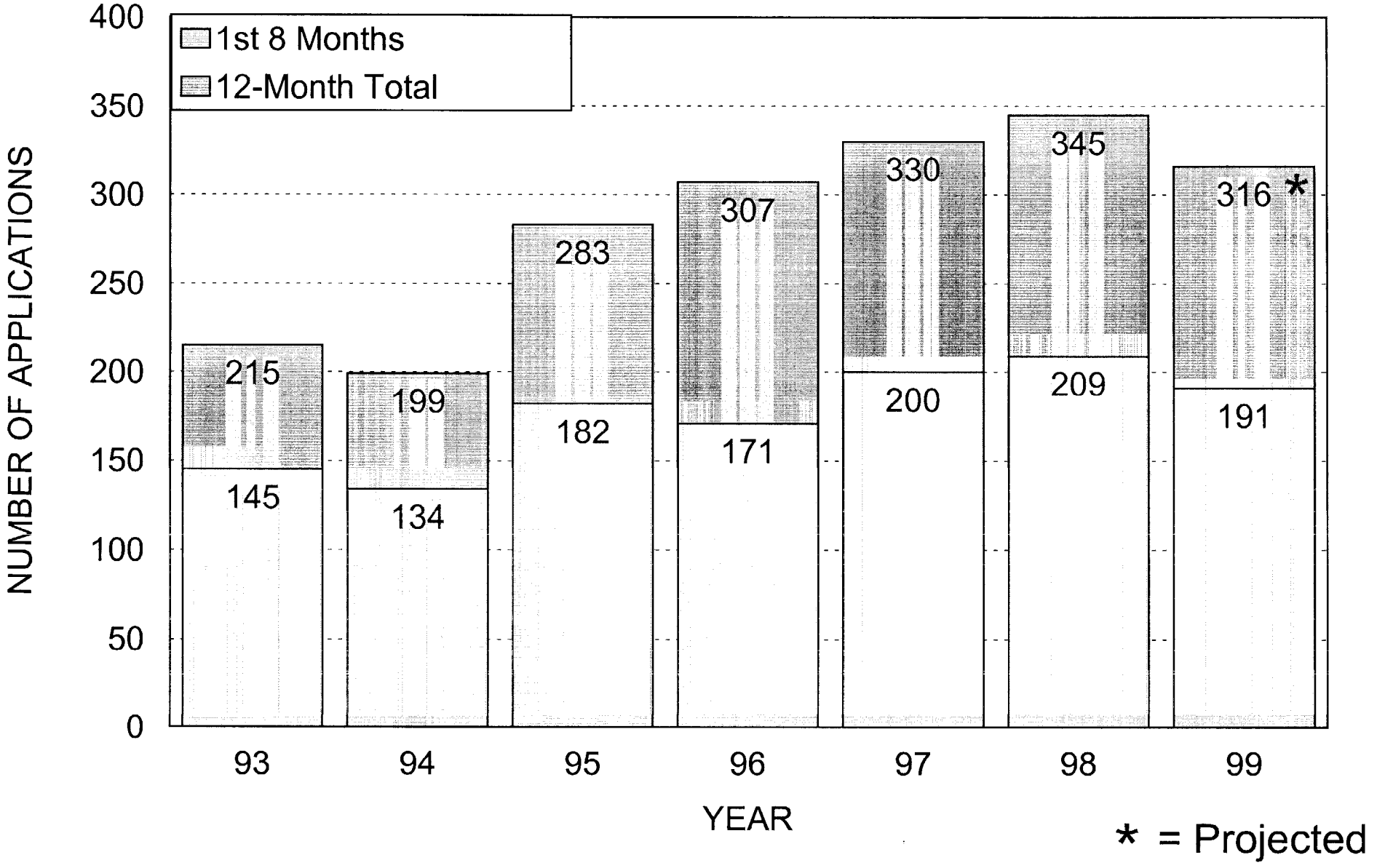
Gary J. Buehler
Deputy Director
Office of Generic Drugs
October 5, 1999
Washington, D.C.

Outline

1. Overview of OGD Performance
2. Performance Improvement
3. Chemistry Guidances
4. Major/Minor Guidance
5. Electronic Labeling Initiatives

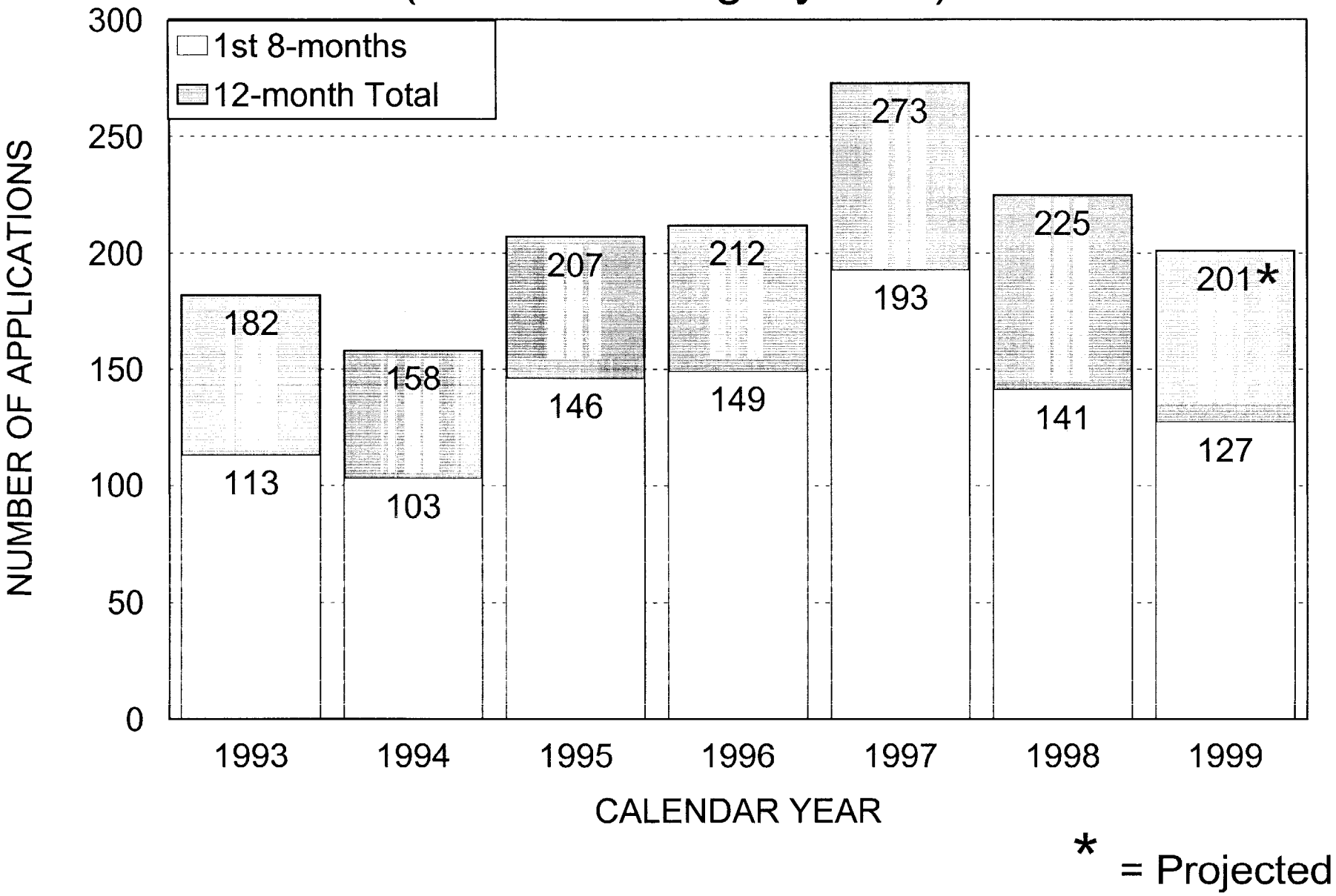
Calendar Year Receipts

(New Counting System)

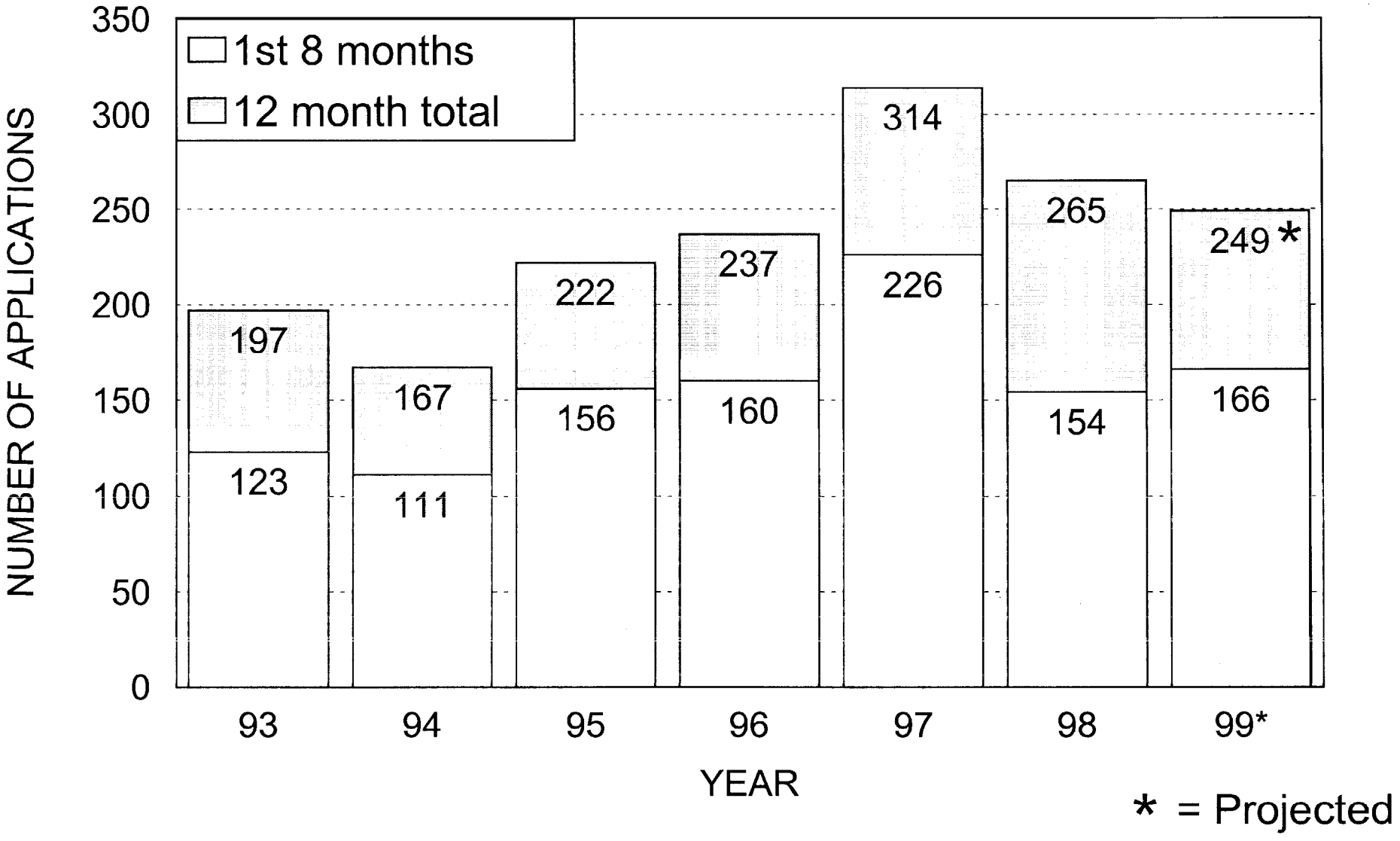


Calendar Year Approvals

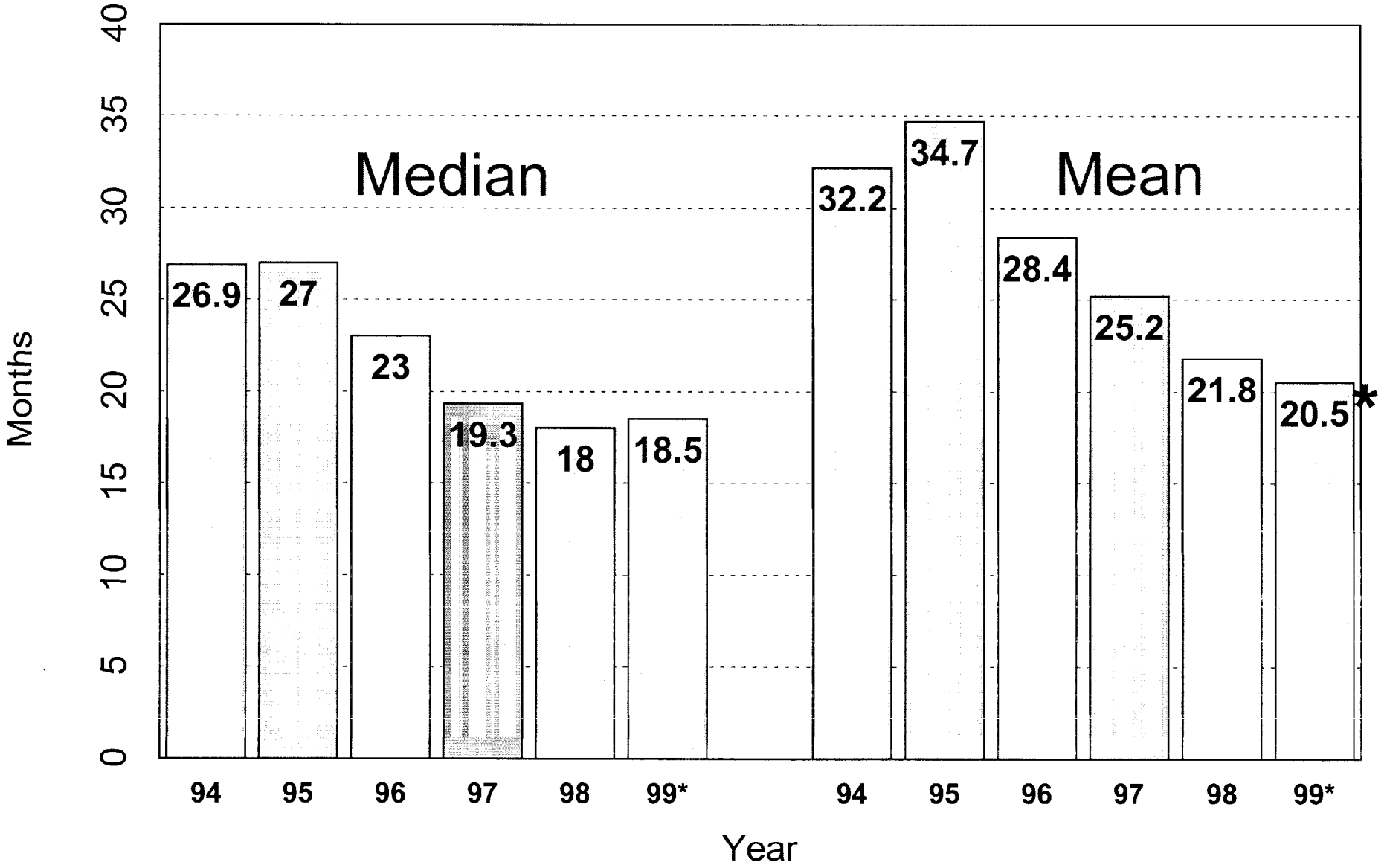
(New Counting System)



Calendar Year Approvals & Tentative Approvals
(New Counting System)



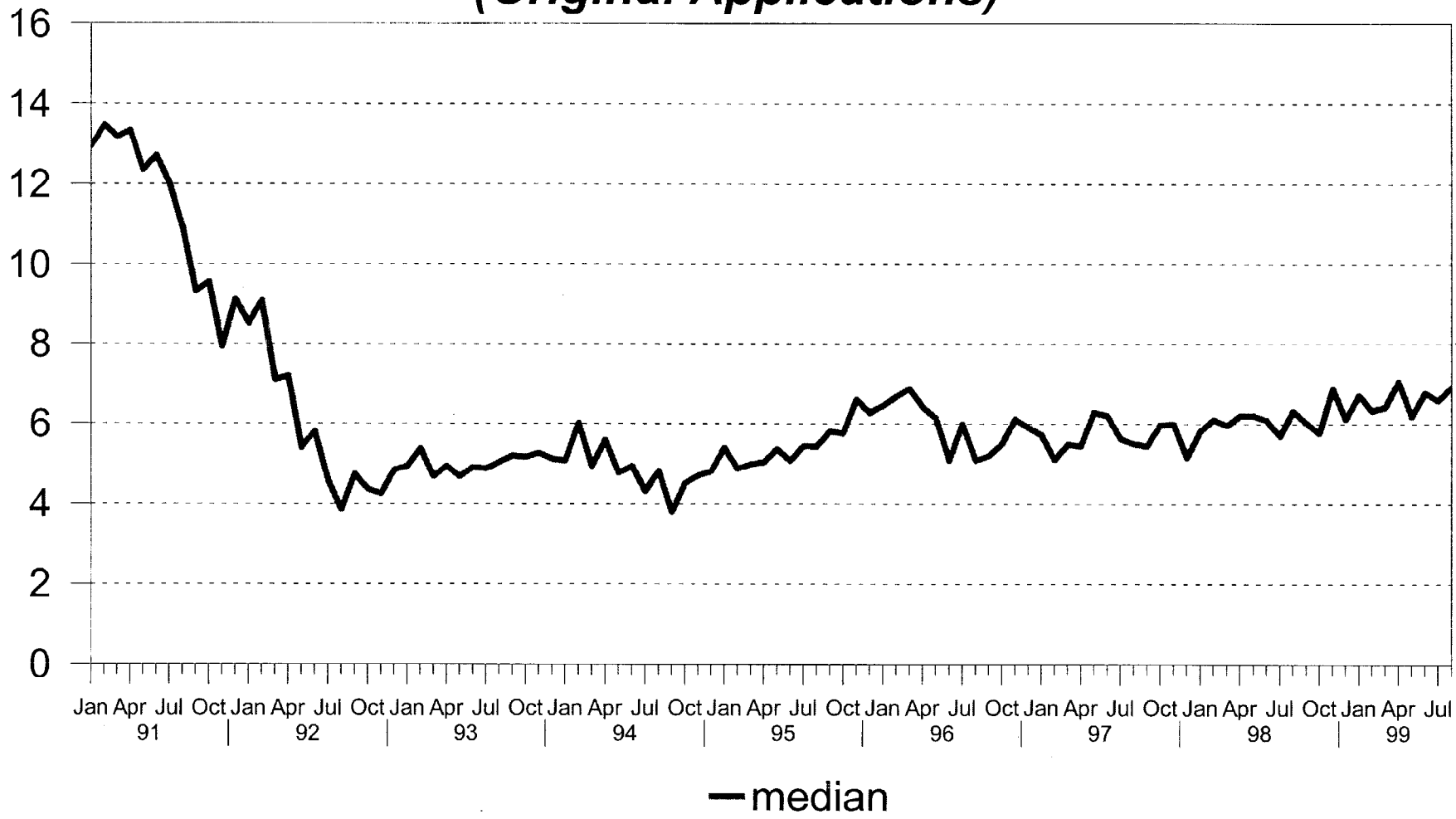
Calendar Year Approval Times



* = Through August 31, 1998

Median ANDA Review Cycle (Months)

(Original Applications)



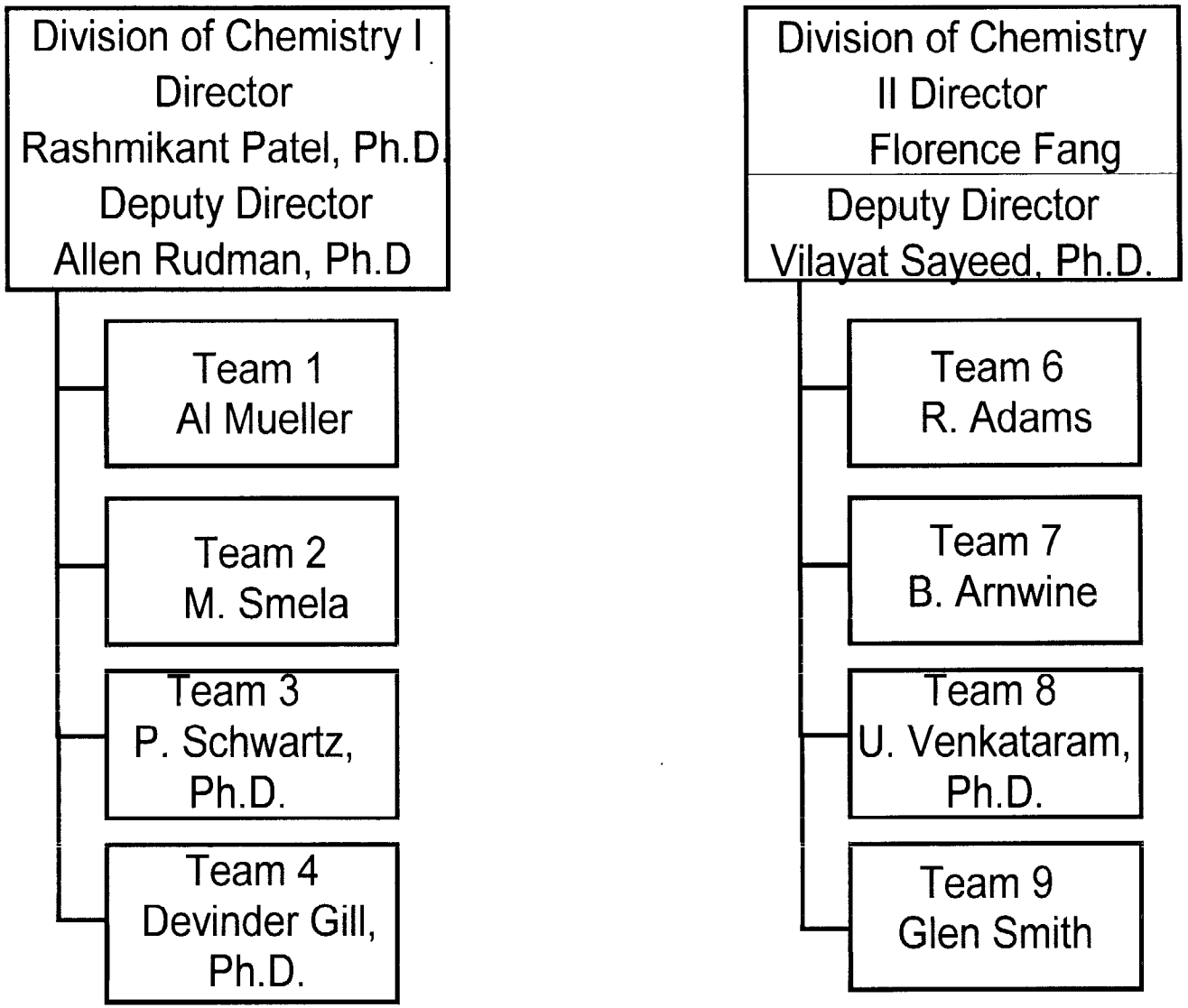
1-Times correspond to actual applications received . The new ANDA/AADA submission policy that went into effect 1/1/91 allows certain variations in a drug product to be included in a single application.

2-In September, 1991 the OGD started implementation of the Application Integrity Policy by suspending review of applications suspected of being tainted by fraud. AIP time has been subtracted from review time above for the period after 9/91. However, before the AIP went into effect, the review of many applications suspected of containing fraudulent data were suspended. These suspensions were not recorded in the MIS and are not reflected in the above chart.

Chemistry is presently the rate-limiting review for ANDA approval.

Present Chemistry Queue
~120 days

Chemistry Divisions Restructuring



ANDAs: Blend Uniformity Analysis

Published: August 27, 1999
Closes: October 26, 1999

Written to address consistency issues regarding review of blend/granulation uniformity in ANDAs. By providing more definite guidance to reviewers and industry, an existing review practice could be more fairly applied.

ANDAs: Impurities in Drug Substances

Published: July 24, 1998
Closed: September 22, 1998
Reopened: Until November 23, 1998

Using principles of the ICH Q3A Impurities in New Drug Substances document, describes impurity qualification and identification criteria for drug substances used in ANDAs.

ANDAs: Impurities in Drug Products

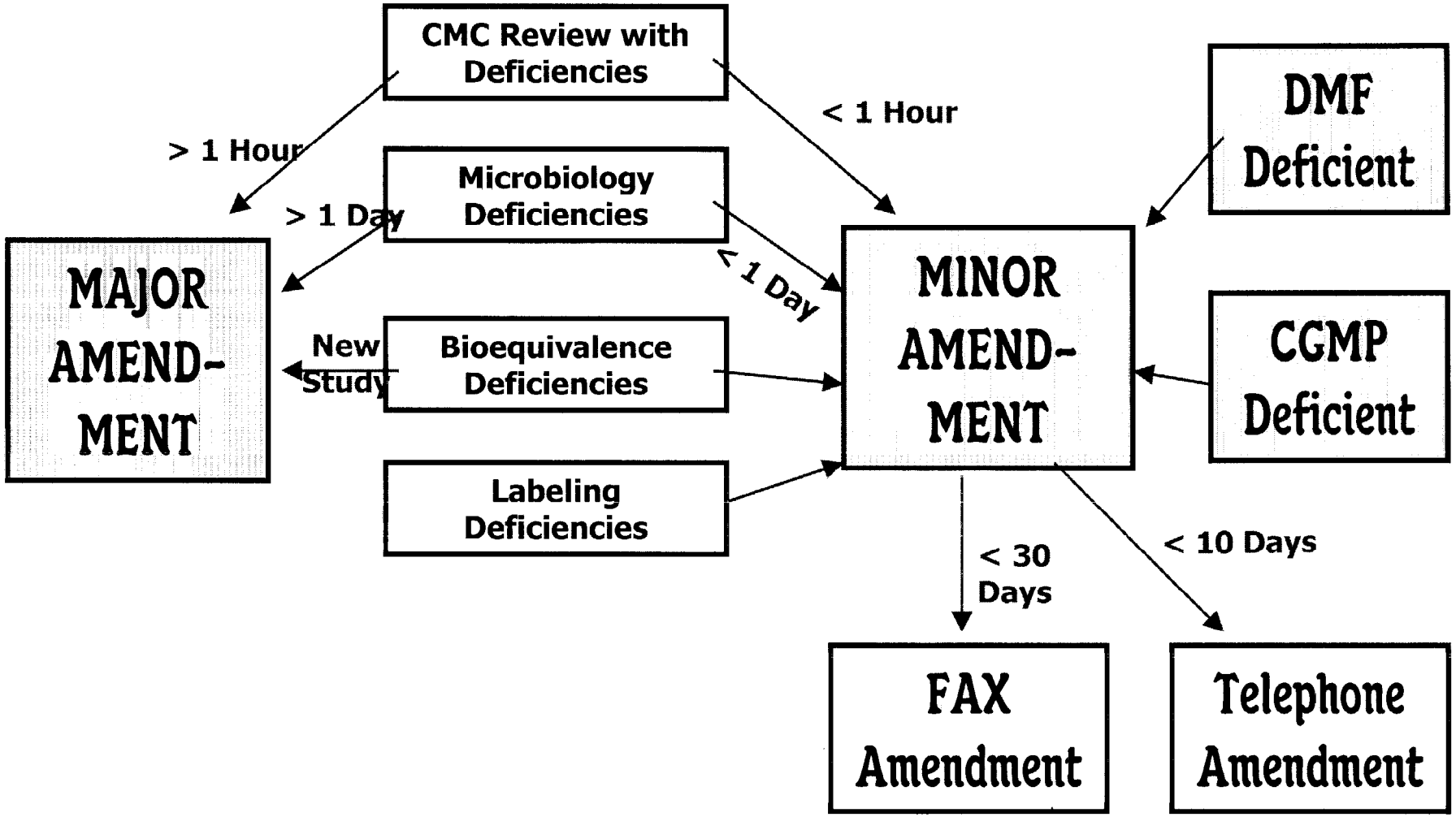
Published: January 5, 1999
Closed: May 5, 1999

Using principles of the ICH Q3B Impurities in New Drug Products document, describes degradant qualification and identification criteria for drug products in ANDAs.

Major, Minor, Facsimile and Telephone Amendments

- Purpose:
  - To present operating policies & procedures to industry
  - To close loopholes arising from FACSIMILE policy
  - Increased control over review clock
  - Standardization throughout OGD
  - Define terminology used to categorize amendments

Major, Minor Amendments



Proposed Electronic Labeling Requirement

- Require the Submission of Electronic Package Insert Text
- NDAs, ANDAs, Supplements, Annual Reports
- Portable Document Format (PDF) - in 8.5 x 11 text

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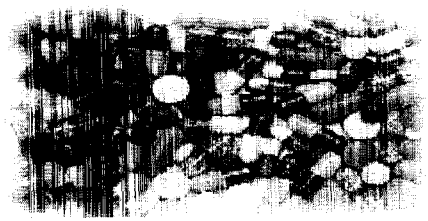

OFFICE OF GENERIC DRUGS (OGD)

Office of Generic Drugs
Division of Labeling and Program Support
Labeling Review Branch
HFD-613

John F. Grace, R.Ph. - Labeling Review Team Leader for Division of Chemistry I
Charles V. Hoppes, R.Ph. - Labeling Review Team Leader for Division of Chemistry II

Phone - (301) 827-5846
Fax - (301) 443-3847

Click on link

The purpose of this page is to provide information on recently approved labeling changes for **Reference Listed Drug** (RLD) products. The supplements are grouped by month and year of approval. Some are linked to the approved labeling and/or the supplemental approval letter in Adobe Acrobat format. Click on a month and year below to view the list for that month:

1999	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug				
1998						Jun	Jul	Aug	Sep	Oct	Nov	Dec

In addition, a comprehensive list of the most recently approved labeling supplements for all RLD products is available in Adobe Acrobat Format. The list is in order of NDA number.

Proposed Electronic Labeling Requirement

- Benefits:
  - Enables Posting of Reference Listed Drug on Web
  - Faster, More Efficient Review

Labeling Review Branch - Microsoft Internet Explorer

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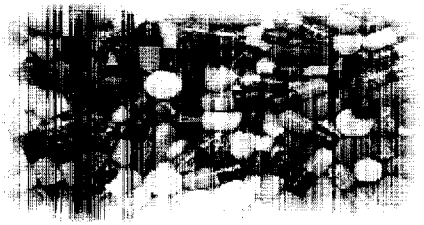

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Internet zone

NDA TRADE NAME INGREDIENT	SPONSOR	RXOTC CODE	DOC TYPE	SUP#	LATEST APPROVAL DATE	ACKNOWLEDGE DATE	A
N000004+ PAREDRINE HYDROXYAMPHETAMINE HYDROBROMIDE	AKORN	RX	SLR	010	08-MAY-80		
N000159+ SULFAPYRIDINE SULFAPYRIDINE	ELI LILLY	RX	SLR	004	28-MAY-86		
N000793+ BUTISOL SODIUM BUTABARBITAL SODIUM	WALLACE LABS	RX	SLR	015	04-NOV-98		
N001546 GUANIDINE HCL GUANIDINE HYDROCHLORIDE	SCHERING	RX	SLR	005	23-SEP-76		
N002282+ INULIN AND SODIUM CHLORIDE INULIN	CYPROS	RX	SLR	016	20-APR-99		I
N003158 ORETON METHYL METHYLTESTOSTERONE	SCHERING	RX	SLR	013	26-JAN-95		I
N003444+ DRISDOL ERGOCALCIFEROL	SANOFI PHARMS	RX	SLR	016	17-APR-86		
N004570+ HEPARIN SODIUM HEPARIN SODIUM	PHARMACIA AND UPJOHN	RX	SLR	054	04-MAR-96	17-APR-96	I
N004589+ ALCOHOL 10% AND DEXTROSE 5% DEXTROSE	B BRAUN	RX	SLR	011	11-OCT-85		
N004782+ PREMARIN ESTROGENS, CONJUGATED	WYETH AYERST LABS	RX	SLR	109	08-JUN-99		

Labeling Review Branch - Microsoft Internet Explorer

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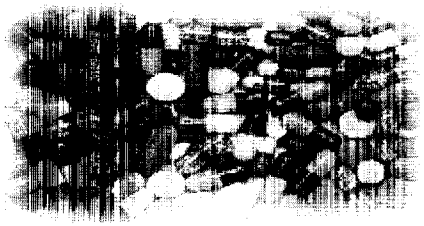

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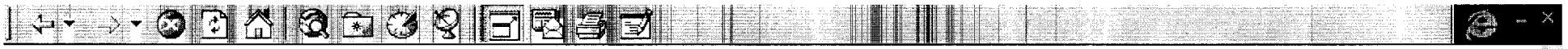

U.S. Food and Drug Administration
Center for Drug Evaluation and Research

Reference Listed Drug Labeling Approved in August 1999

Some of the product names below contain links to the approved labeling or the supplemental approval letter describing the specific changes. Click on the product name to view the approved labeling changes in Adobe Acrobat format.

Product Name	Drug Name	NDA No	Supp.No	Firm	Date
LARIAM	Mefloquine HCl Tablets	19-591	S-012	Roche	02-Aug-1999
PROSCAR	Finasteride Tablets	20-180	S-018	Merck	02-Aug-1999
CEFOTAN	Cefatetan Disodium	50-588	S-026	Zeneca	05-Aug-1999
MARINOL	Dronabinol Capsules	18-651	S-011	Unimed	05-Aug-1999
ZOCOR	Simvastatin Tablets	19-766	S-032	Merck	05-Aug-1999
GLUCOTROL	Glipizide Tablets	17-783	S-015	Pfizer	06-Aug-1999
PROLOPRIM	Trimethoprim Tablets	17-943	S-015	Monarch Pharms	06-Aug-1999
PRANDIN	Repaglinide Tablets	20-741	S-001	Novo Nordisk Pharm	10-Aug-1999
DROXIA	Hydroxyurea Capsules	16-295	S-026	Bristol Myers Squibb	11-Aug-1999
HYDREA	Hydroxyurea Capsules	16-295	S-026	Bristol Myers Squibb	11-Aug-1999
IDAMYCIN PFS	Idarubicin HCl Injection	50-734	S-004	Pharmacia &Upjohn	12-Aug-1999
AZULFIDINE	Sulfasalazine Tablets	07-073	S-110	Pharmacia & Upjohn	13-Aug-1999
AZULFIDINE EN-TABS	Sulfasalazine Tablets	07-073	S-110	Pharmacia &Upjohn	13-Aug-1999
PREPIDIL	Dinoprostone Gel	19-617	S-002	Pharmacia &Upjohn	13-Aug-1999
ZAROXOLYN	Metolazone Tablets	17-386	S-030	Medeva Pharms	13-Aug-1999
RESCRIPTOR	Delavirdine Mesylate Tablets	20-705	S-004	Pharmacia &Upjohn	16-Aug-1999
BENTYL	Dicyclomine HCl Injection	08-370	S-028	Hoechst Marion Rssl	17-Aug-1999
BENTYL	Dicyclomine HCl Syrup	07-961	S-025	Hoechst Marion Rssl	17-Aug-1999
BENTYL	Dicyclomine HCl Tablets	07-409	S-039	Hoechst Marion Rssl	17-Aug-1999
DERMA-SMOOTHE/FS	Fluocinolone Acetonide Sol.	19-452	S-015	Hill Derm	18-Aug-1999
EULEXIN	Flutamide Capsules	18-554	S-015	Schering	19-Aug-1999
MEPERGAN	Meperidine HCl/Promethazine HCl	11-730	S-023	Wyeth Ayerst Labs	19-Aug-1999
ALDOCLOR-250	Methyldopa/Chlorthiazide Tablets	16-016	S-070	Merck	22-Aug-1999

Click on links

NDA 7-409/S-039
NDA 8-370/S-028
NDA 7-961/S-025

AUG 17 1999

Hoechst Marion Roussel
Attention: Kim Leitzke
10236 Marion Park Drive, P.O. Box 9627
Kansas City, MO 64134

Dear Ms. Leitzke:

Please refer to your supplemental new drug applications dated April 2, 1999, received April 5, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Bentyl (dicyclomine hydrochloride USP) Tablets/Capsules, Injection, and Syrup.

We note that these supplements were submitted as 'Special Supplement - Changes Being Effected' under 21 CFR 314.70(c).

These supplemental new drug applications provide for the revision of the **OVERDOSAGE** section of the package insert to include a description of a 15 Day adverse event report in which a 37 year old female reported numbness, cold fingertips, abdominal pain, decreased appetite, dry mouth, and nervousness following the ingestion of 320 mg daily for several days. Your submission stated March 18, 1999 as the implementation date for the change.

We have completed the review of these supplemental applications, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the final printed labeling submitted April 2, 1999. Accordingly, these supplemental applications are approved effective on the date of this letter.

If a letter communicating important information about these drug products (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

Page thru document or Click on links